REMARKS

Claims 72-82 and 85-88 were pending in the present application. Claims 85 and 86 are withdrawn from consideration. Accordingly, claims 72-82 and 87-88 are currently pending.

Applicants thank the Examiner for withdrawing all rejections except the 35 U.S.C. § 112, first paragraph rejection, in view of the Applicant's amendments and arguments.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 72-82 and 87-88 are rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner stated that "there is insufficient guidance and or objective evidence that supports the inhibition of cancer cell growth, viability, and or survivability comprising administering an anti-TMPRSS2 antibody, either in-vitro or in-vivo."

In response, Applicants hereby submit the declaration of Dr. Arthur Raitano, Ph.D. This declaration is referred to as the "2004 Raitano declaration" (or the "2004 declaration") to distinguish it from the declaration of Dr. Raitano submitted with the response filed on November 20, 2003. Dr. Raitano's declaration describes experiments demonstrating the effect of an anti-TMPRSS2 monoclonal antibody designated M9-5.1 on the growth of LNCaP prostate cancer cells, either by itself, or conjugated to a toxin. The data is presented in Exhibits B and C which accompany the declaration. Paragraph 5 of Dr. Raitano's 2004 declaration indicates that experiments were conducted with a monoclonal antibody against TMPRSS2 designated M9-5.1.

The data clearly show that, in this *in vitro* system, the monoclonal antibody can inhibit the growth of the cancer cells. Paragraph 6 of the 2004 Raitano declaration reports that, at a concentration of 40 μg/ml, the M9-5.1 antibody against TMPRSS2 demonstrated an inhibitory effect on the growth of the LNCaP prostate cancer cell line, as compared with a control antibody

against keyhole limpet hemocyanin (anti-KLH control antibody). See Exhibit B of the 2004 Raitano declaration.

When the M9-5.1 antibody was used in conjunction with a second antibody which binds to IgG, where the second antibody was in turn bound to the toxin saporin, the results were even more significant. The anti-TMPRSS2 M9-5.1 antibody/anti-mouse IgG antibody/saporin toxin complex showed more inhibitory effect than the anti-KLH (control) antibody/anti-mouse IgG antibody/saporin toxin complex, even at concentrations as low as 1.6 ng/ml of antibody complex. See Exhibit C of the 2004 Raitano declaration.

Applicants thus submit that there is objective evidence that supports the inhibition of cancer cell growth, viability, and/or survivability when practicing the invention according to the instant claims.

The 2004 Raitano declaration quite clearly demonstrates that claims 87-88 are enabled. These claims are limited to *in vitro* administration of an antibody or fragment thereof to the cancer cells. The 2004 Raitano declaration shows that antibodies against 20P1F12/TMPRSS2 are capable of inhibiting the growth, viability and/or survivability of cancer cells that express a 20P1F12/TMPRSS2 protein. Applicants respectfully request withdrawal of the rejection with respect to claims 87-88.

Applicants also submit that the declaration provides evidence that claims 72-82 are enabled, and thus allowable. The Manual of Patent Examining Procedure, at MPEP 2164.06(a) III., discussing examples of enablement issues, refers the reader to MPEP 2107-2107.03 for a "discussion of the utility requirement under 35 U.S.C. 112, first paragraph, in drug cases." This section of the MPEP indicates that "[a]s a general matter, evidence of pharmacological or other biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility." (MPEP 2107.03 I., citations omitted; emphasis in original.) That section of the MPEP goes on to state "[t]he applicant does not have to prove that a correlation exists between a particular activity and an asserted

therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use." ((MPEP 2107.03 I., citations omitted.)

Applicants submit that such a reasonable correlation does exist. The 1999 article by Weiner, "An overview of monoclonal antibody therapy of cancer," Semin. Oncol. 26(4 Suppl 12):41-50, states in its abstract that "[m]onoclonal antibody-based therapeutics are beginning to realize the promise that was predicted with the advent of the core technology more than 20 years ago. Antibody-based therapeutics targeting tumor cell surface antigens such as B-cell idiotypes, CD20 on malignant B cells, CD33 on leukemic blasts, and HER2/neu on breast cancer cells have shown efficacy in clinical trials." This article was cited by the Examiner in the Office Action dated August 23, 2002 (Paper No. 34). While Weiner mentions certain challenges that antibody therapy faces, as the MPEP states, *statistical certainty* is not required, only a reasonable correlation, which is indicated in the Weiner article.

In view of the evidence assembled and the appropriate legal standard, Applicants submit that claims 72-82 and 87-88 are allowable. An early notice to that effect is earnestly solicited.

CONCLUSION

In view of the above remarks, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no.511582000800. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: December 15, 2004

Respectfully submitted,

By _____

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